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EXAMINER

SAUNDERS, DAVID A

ART UNIT PAPER NUMBER

1644

DATE MAILED: 11/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

121,017

Applicant(s)

IMANURA et al

Examiner

SAUNDERS

Group Art Unit

1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 5/5/03 & 7/24/03
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1, 3-6, 14, 17-21, 23-28 is/are pending in the application.
- Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1, 3-6, 14, 17-21, 23-28 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Other _____

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Amendment of 5/15/03 and the response of 7/24/03 have been entered
the amendment has entered no new matter.

Claims 1, 3-6, 14, 17-21 and 23-28 are pending and under examination.

Applicant is reminded that the substitute specification filed 3/29/02 has not
been entered.

The text of those sections of Title 35, U.S. Code not included in this action can
be found in a prior Office action.

Except as noted below, the amendment has overcome previously stated
rejections under 112, first and second paragraphs.

Claims 1, 3-6, 14, 17-21 and 23-28 are rejected under 35 U.S.C. 112,
second paragraph, as being indefinite for failing to particularly point out and
distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 19-20 are each unclear by reciting "the residual activity" for
three reasons.

First, it is not clear what kind of "activity" is intended. Is it the heparin
binding activity or some other activity of the protein (e.g. growth promoting
activity of FGF)? From what can be gleaned from the disclosure it appears that
the latter is intended.

Second, "residual" is unclear since it is not clear what the "residual
activity" is compared against. What is the "baseline" or 100% activity, which
serves as a comparison standard against which the "residual activity" is
compared? It is not even clear as to whether the protein, which serves as a

comparison standard, is glycosylated or not. It appears, from the examples, that applicant may intend the comparison standard is glycosylated.

Third, it is not clear if there is some process or treatment that the protein is subjected to, prior to determining how much "residual activity" remains. From page 5, it appears that applicant might be contemplating some sort of destabilizing process.

The amendment has not changed this phrase and has not argued why "residual activity" is definite.

In each independent claim the third and fourth members of the Markush group if sugar chains are unclearly recited. In reciting an "O-linked (or N-linked) sugar chain combined with a sulfated polysaccharide or glycosaminoglycan" it is not clear how these are "combined". The examiner can envision two ways: 1) the O-linked sugar chain and the sulfated polysaccharide or glycosaminoglycan are each separately bonded to the protein/peptide, or 2) the O-linked sugar chain is further linked to the sulfated polysaccharide or glycosaminoglycan. (i.e. the sulfated polysaccharide or glycosaminoglycan is indirectly linked to the protein/peptide). The examiner cannot find a description of either embodiment in the original disclosure (See 112 first further infra), thus one has no idea what applicant is claiming.

Applicant's amendment that has inserted a comma between the fourth and fifth Markush members does nothing to overcome the indefiniteness concerning the nature of how of the O-linked or N-linked sugar chain is combined with a

sulfated polysaccharide or glycosaminoglycan. Even if the same phrase were recited in the specification (112 first infra), this would not overcome indefiniteness, because a phrase can be indefinite, irrespective of whether or not it is in the specification or claims.

Independent claim 23 is unclear in reciting "the activity" (lines 5 and 6). As noted supra regarding recitations of "residual activity" is intended.

For like reasons recitation of "activity" is unclear in claim 6.

As noted supra, with respect to claims 1 and 19-20, the response has done nothing to address the issue of indefiniteness regarding recitation of "activity".

Claims 4, 16 and 18-19 are each unclear by reciting "through a peptide". Likewise claim 20 is unclear by reciting, "containing a peptide sequence". In each claim it is uncertain how the "peptide" is structurally related to the heparin binding protein; note, in claim 20, "containing a peptide" could be read as part of the amino acid sequence inherent to the structure of the heparin binding protein. Otherwise, if "peptide" is a sequence added to the heparin binding protein, it is unclear as to how this is added —e.g. fused via a peptide bond, or bridged via a disulfide bond? The disclosure (e.g. pages 7, 9-11) appears to only describe the former case bond, or bridged via a disulfide bond? The disclosure (e.g. pages 7, 9-11) appears to only describe the former case.

The examiner finds that the amendment has not changed this recitation and has not argued why the phrases "through a peptide" and "containing a peptide sequence" are definite.

The term "near one of the ends" in claim 6 is a relative term which renders the claim indefinite. The term "near one of the ends" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The claims and disclosure give no direction as to how many residues away from the "end" one can add the sugar chain and still be considered "near" to one of the ends. Also it is not clear if this addition must be at a residue within the heparin binding protein, or if it can be at a residue of a peptide fused thereto.

Applicant's response has not amended claim 6 and has not explained why "near" is definite.

Claims 1, 3-6, 14, 17-21 and 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims contain new matter.

In each independent claim the third and fourth members of the Markush group of sugar chains contain new matter. Specifically these were originally

recited as simply "an O-linked sugar chain, an N-linked sugar chain"; without any recitations of "combined with a sulfated polysaccharide or glycosaminoglycan".

There was nothing in the originally filed disclosure that pointed to such a combination of an O- or N-linked sugar chain with a sulfated polysaccharide or glycosaminoglycan, Applicant is therefore greeting a new subspecies of Markush group members was not originally contemplated.

Applicant has traversed this rejection by indicating that page 4, line 16; page 5, line 3 and page 7, line 28 – page 8 line 12 support. The examiner fails to find literal, *ipsis verbis* support therein. If applicant deems that "and a combination thereof" supports then the examiner wonders why applicant has bothered to amend the claims to recite the third and fourth members as he now does. The claims recite "and this recitation encompasses what was disclosed in the specification in terms of combinations. The claims recite "and combinations thereof" anyway; thus this recitation encompasses what was disclosed in the specification in terms of combinations. The examiner maintains that what is now recited is a recitation of a new subspecies of Markush group number(s).

Also, given the above noted ambiguity (112, second rejection) pertaining to the manner in which the N- or O-linked sugar is "combined" with a sulfated polysaccharide or sulfated polysaccharide or glycosaminoglycan, the claims are considered as encompassing new matter, if they are interpreted according to the second option put forward by the examiner (112, second *supra*). That is, everything discussed in the specification pertains to N- or O- linked sugars joined

to an amino acid side chain within the protein/peptide (e.g. page 7, line 3 – page 11, line 11).

Claim 23 recites new matter by reciting, “wherein the activity of the heparin binding protein is greater than the activity of the unmodified protein”. The examiner cannot find any *ipsis verbis* support for this phrase, and no inherent support. Rather, it appears from page 5 and from the examples that applicant has disclosed that the modified proteins have improved stability over the unmodified proteins.

The amendment has not changed this phrase and has not argued why this phrase is not new matter.

Claims 1, 3-6, 14, 17-21 and 23-28 are rejected under 35 U.S.C. 102(e) as being entirely anticipated by Saunders et al. (5,486,599), for reasons of record.

Applicant has merely traversed the prior art rejection by alleging that Saunders et al. present speculative assertions regarding various combinations of molecules and that Saunders et al. provide a non-enabling disclosure. No factual arguments are presented by an expert (e.g. in 1.132 declaration form) to demonstrate that Saunders et al. do not, in fact, enable their invention. Even, if such a declaration were to be presented it would not be persuasive, since Saunders et al. claim what applicant claims, and what has been issued to Saunders et al is presumed valid with respect to all statutes. Note claim 20 of Saunders et al. reciting “a syndecan/basic FGF fusion protein”. Applicant clearly considers FGF as a heparin binding protein (specification page 6) and clearly

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contemplates syndecan as a peptide, which can undergo addition of a sulfated polysaccharide (specification page 10).

Applicant's arguments filed 5/15/03 have been fully considered but they are not persuasive for the above reasons.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday - Thursday from 8:00 a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The

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fax phone number for the organization where this application or proceeding is assigned is (703)872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr
October 17, 2003

David A. Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182/644